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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 12/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,651	SCHOR ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7-9,29 and 60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4,5 and 29* is/are allowed.

6)☒ Claim(s) *1,7-9 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 21, 2006, has been entered.

1. The amendment filed September 21, 2006, is acknowledged and has been entered. Claim 61 has been canceled. Claims 1 and 9 have been amended.

2. Claims 1, 4, 5, 7-9, 29, and 60 are currently under prosecution.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Allowable Subject Matter

4. Claims 4, 5, and 29 are allowable.

Priority

5. As explained in the preceding Office action, although Applicant has claimed the benefit of the earlier filing date under 35 USC § 120 of the PCT Application No. PCT/GB98/03766, filed December 15, 1998, which in turn claims benefit of United Kingdom Patent Application No. 9726539.1, filed December 16, 1997, claims 1, 7-9, and 60 do not properly benefit, because those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description and a sufficiently enabling disclosure. In particular, it is noted the subject matter of claims 1, 7-9, and 60 is not adequately described in the prior applications, as neither application teaches a

genus of polynucleotides having at least 95% identity to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 41, which has at least 30% of the migration stimulation factor activity of a polypeptide having the amino acid sequence of SEQ ID NO: 2. Although the specifications of the prior applications describe polynucleotides encoding a polypeptide comprising SEQ ID NO: 2, neither specification describes the far broader genus of polynucleotides encoding polypeptides comprising SEQ ID NO: 41. This issue is further addressed below in the new rejection of claims 1, 7-9, and 60, as failing to satisfy the written description requirement.

As previously explained, to receive benefit of the earlier filing date under 35 USC § 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Accordingly, the effective filing date of the claims 1, 7-9, and 60 is deemed the filing date of the instant application, namely October 10, 2000.

Applicant has notably argued, because this application was filed under 35 U.S.C. § 371, the filing date of this application should be considered December 15, 1998, as opposed to October 10, 2000 (amendment filed September 21, 2006; page 4, paragraph 3). In response, this application was filed in the U.S. as the National stage entry of the earlier filed International application on October 10, 2000; and as explained above, it does not properly benefit from the earlier filing date of the International application, since, for example, the claims are directed to subject matter not described in the earlier filed application, which accordingly would fail to provide a written description of the subject matter that is now claimed in the instant application, so as to satisfy the requirements set forth under 35 U.S.C. § 112, first paragraph.

Grounds of Objection and Rejection Withdrawn

6. Unless specifically reiterated below, Applicant's amendment and/or arguments filed September 21, 2006, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed June 22, 2006.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

7. The rejection of claims 1, 7-9, and 60 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "new matter" rejection.

Beginning at page 4 of the amendment filed September 21, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Claim 1, as presently amended, recites, "a polynucleotide with at least 95% sequence identity [to an isolated recombinant polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2] encoding a polypeptide comprising the amino acid sequence of VSIPPRNLGY (SEQ ID NO: 41), said polypeptide having at least 30% of the migration stimulation factor activity of a polypeptide having the amino acid sequence of SEQ ID NO:2 [...]".

Applicant has asserted that support for the amendment to the claims is found in the specification filed June 3, 2005, at page 9, lines 19-25.

However, contrary to Applicant's assertion, the disclosure at page 9, lines 19-25, does not appear to provide written support for the language of the instant claims.

Although the specification, as originally filed, describes two polypeptides (i.e., the polypeptide of SEQ ID NO: 2, and the immunogenic, synthetic peptide of SEQ ID NO: 5), which comprise the amino acid sequence of SEQ ID NO: 41, the specification has not described with any degree of particularity a genus of nucleic acid molecules

encoding a genus of polypeptides comprising this amino acid sequence, which have at least 30% of the ability of a polypeptide comprising SEQ ID NO: 2 to stimulate migration of adult skin fibroblasts into a collagen gel. Furthermore, while at page 46 of the substitute specification filed June 8, 2005, there is a description of monoclonal antibodies, which are raised using immunogens that are synthetic peptides based on the 10 amino acid unique tail of MSF (i.e., the amino acid sequence of SEQ ID NO: 41), or on any of the peptide sequences of SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9, this description does not suffice to provide proper and sufficient support for the language of the claims because it does not describe a genus of polypeptides comprising the amino acid sequence of SEQ ID NO: 41, which have at least 30% of the ability of a polypeptide comprising SEQ ID NO: 2 to stimulate migration of adult skin fibroblasts into a collagen gel.

Again, this issue might be resolved if Applicant were to point to particular disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary support for the language of the present claims.

8. The rejection of claims 1, 7-9, and 60 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

Beginning at page 4 of the amendment filed September 21, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001;

hereinafter, the "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

The claims are not drawn to a genus of polypeptides that are 95% identical to the polypeptide of SEQ ID NO: 2; rather the claims are directed to a genus of nucleic acid molecules comprising a polynucleotide sequence that is 95% identical to another nucleic acid molecule, which encodes a polypeptide comprising SEQ ID NO: 2. The members of this genus of nucleic acid molecules to which the claims are directed necessarily encode a polypeptide comprising the amino acid sequence of SEQ ID NO: 41, which has at least 30% of the migration stimulation factor activity of a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, but SEQ ID NO: 41 is only 10 amino acids in length and, as previously noted, is not described as a substantial structural feature of the polypeptide of SEQ ID NO: 2 or any variant thereof, which correlates with the polypeptides' abilities to act as migration stimulation factors. For example, there is no indication or factual evidence disclosed, which teaches or even suggests a peptide consisting of the amino acid sequence of SEQ ID NO: 41 is capable of acting as the full-length polypeptide comprising SEQ ID NO: 2. Thus, given the structural disparity of the polypeptides encoded by the members of the claimed genus of nucleic acid molecules, it is apparent that the polynucleotide sequence of SEQ ID NO: 3, which is described as encoding the amino acid sequence of SEQ ID NO: 2, is not representative of the claimed genus, as a whole, and consequently the skilled artisan could not immediately envision, recognize or distinguish at least a substantial number of its members. For this reason, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

Furthermore, "generalized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that

adequately describes with the requisite degree of particularity the genus of polypeptides comprising the amino acid sequence of SEQ ID NO: 41, which have at least 30% of the migration stimulation factor activity of a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. A description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

In addition, although the skilled artisan could initially screen candidate peptides and polypeptides comprising the amino acid sequence of SEQ ID NO: 41 to identify those that have at least 30% of the migration stimulation factor activity of a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 by empirically determining their ability, or lack thereof, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating (or identifying) it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

"Guidelines" (cited *supra*) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of polypeptides, which vary structurally, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings,

or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. In this instance, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; Applicant has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; and Applicant has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

9. The rejection of claims 1, 7-9, and 60 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** an isolated, recombinant nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, an isolated, recombinant nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 3 from the nucleotide at position 57 through the nucleotide at position 1982, an isolated replicable vector comprising any of said polynucleotide sequences, an isolated host cell comprising said vector, and a method for producing said polypeptide by a process comprising culturing said host cell and isolating said polypeptide, or any nucleic acid molecule taught by the prior art, **does not reasonably provide enablement for making and using** an isolated nucleic acid molecule having a polynucleotide sequence that is at least 95% identical to a polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 41 and having at least 30% of the migration stimulation factor activity of a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, an isolated replicable vector comprising said polynucleotide sequence, an isolated host cell comprising said polynucleotide sequence, or a method for producing a polypeptide encoded by said nucleic acid molecule, said method comprising culturing a host cell comprising the polynucleotide sequence of said nucleic acid molecule and isolating the polypeptide. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make/or the invention commensurate in scope with these claims.

Beginning at page 5 of the amendment filed September 21, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued the claimed invention could be made and used without reliance upon predictions and undue experimentation. The Examiner disagrees. As explained above, the claims are directed to a genus of structurally disparate polypeptides that have at least 30% of the migration stimulation factor activity of a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. Although the polypeptides necessarily comprise the amino acid sequence of SEQ ID NO: 41, a peptide consisting of this amino acid sequence does not have the requisite activity of the claimed polypeptide, as there is no disclosure teaching or suggesting that such a peptide is capable of functioning in a manner similar to the full-length polypeptide comprising SEQ ID NO: 2. Contrary to Applicant's assertions, it would not be possible to rely upon *predictions*, as it is well established that the artisan cannot predict whether a polypeptide comprising the amino acid sequence of SEQ ID NO: 41 has at least 30% of the migration stimulation factor activity of a polypeptide comprising the amino acid sequence of SEQ ID NO: 2; accordingly, to practice the claimed invention, the artisan would have to empirically determine whether any given polypeptide comprising SEQ ID NO: 41 would be so capable. The claimed invention could not be made or used without first performing such empirical determinations, and that need falls well within the realm of undue and unreasonable experimentation.

M.P.E.P. § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person

skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

In conclusion, careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), reveals a preponderance of factual evidence of record that indicates the disclosure would not be sufficient to have enabled the skilled artisan to make the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 102

10. The rejection of claims 1, 7-9, and 60 under 35 U.S.C. 102(b), as being anticipated by WO 99/31233 A1, is maintained.

At page 8 of the amendment filed September 21, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

As explained in the preceding Office action, WO 99/31233 A1 (Schor et al.) teaches a polynucleotide encoding a polypeptide comprising an amino acid sequence identical to SEQ ID NO: 2, which comprises the amino acid sequence of SEQ ID NO:

41; see entire document (e.g., claim 18). Furthermore, Schor et al. teaches the polypeptide has migration stimulating factor activity and elicits antibodies that bind to the polypeptide but not to fibronectin; see, e.g., claims 6 and 27. In addition, Schor et al. teaches an isolated replicable vector comprising a polynucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to SEQ ID NO: 2; see, e.g., claim 7. Schor et al. teaches an isolated host cell comprising a polynucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to SEQ ID NO: 2; see, e.g., claim 8. Schor et al. teaches making a polypeptide comprising an amino acid sequence identical to SEQ ID NO: 2 by a process that comprises transfecting a host cell with a polynucleotide encoding the polypeptide, or a vector comprising such a polynucleotide, and isolating the polypeptide; see, e.g., claim 9.

Because the amino acid sequence of the disclosed polypeptide is identical to SEQ ID NO: 2, the disclosed polypeptide is expected to have 100% of the migration stimulation factor activity of a polypeptide having such an amino acid sequence, wherein said activity refers to the ability to stimulate adult skin fibroblast migration into a collagen gel.

Applicant has argued the reference is not prior art; but to the contrary, as explained above, the effective filing date of the instant claims is October 10, 2000; therefore, the reference is prior art under 35 U.S.C. 102(b).

Applicant's argument has thus been carefully considered but not found persuasive.

Claim Rejections - 35 USC § 103

11. The rejection of claims 1, 7-9, and 60 under 35 U.S.C. 103(a), as being unpatentable over Grey et al. (of record), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, in view of Bendig (of record), is maintained.

Beginning at page 6 of the amendment filed September 21, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued Grey et al. does not disclose any particular sequences, and does not suggest a polypeptide, which comprises the particular sequence of SEQ ID NO: 41. In response, the claims are not directed to any one particular polynucleotide but rather to any nucleic acid molecule encoding a polypeptide having the recited structural and functional features. Given the conventional and routine nature of the methodology used to isolate polynucleotides encoding a polypeptides at the time the invention was made, there is no reason believe such a polynucleotide would not have been obtained.

Furthermore, as explained in the preceding Office action, the claims are directed to a genus of structurally varying nucleic acid molecules having at least 95% identity to a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which encode polypeptides comprising the amino acid sequence of SEQ ID NO: 41 and have the recited functional characteristic. Encompassed by the claims is a nucleic acid molecule encoding the polypeptide of SEQ ID NO: 2. As explained in the above rejection of claim 9 under 35 U.S.C. 102(b), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, the 70 kDa polypeptide designated "migration stimulation factor (MSF)", which was isolated from cultured fibroblasts by Grey et al., is the polypeptide of SEQ ID NO: 2. Grey et al. teaches, "[o]ur current efforts are directed toward cloning the gene for MSF and obtaining its complete sequence" (page 2441, column 1). Therefore, again, it would have been obvious to one ordinarily skilled in the art at the time the invention was made to have cloned a nucleic acid molecule encoding the polypeptide disclosed by Grey et al. (i.e., the polypeptide of SEQ ID NO: 2) because Grey et al. teaches efforts are underway to do exactly that, and Bendig teaches the methodology necessary to do so was well within the skill of the artisan of ordinary skill at the time the invention was made. Accordingly, as also previously explained, it would have been obvious to one ordinarily skilled in the art at the time of the invention to produce a host cell comprising a vector comprising the

cloned polynucleotide sequence encoding the polypeptide by recombinant DNA technology in accordance with the teachings reviewed by Bendig and then culture the host cells and isolate the polypeptide produced by the host cells in the culture. Therefore, among other reasons, one ordinarily skilled in the art at the time of the invention would have been motivated to do so to facilitate production of the polypeptide by recombinant means.

Claims 4 and 5, which are specifically drawn to a nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 3 or a specific portion thereof, are not rejected as being obvious, since the precise cDNA molecule of claims 4 and 5 would not have been obvious over the Grey et al. teaching of the isolated polypeptide. As Applicant has correctly noted, the redundancy of the genetic code precludes contemplation of or focus on the specific cDNA molecules. What cannot be contemplated or conceived cannot be obvious. See *In re Deuel*, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995).

However, to the contrary, a genus of nucleic acid molecules comprising a polynucleotide sequence encoding a polypeptide comprising SEQ ID NO: 2 *can be contemplated and conceived.*

"A claim to the genus of DNA molecules complementary to the RNA having the sequences encompassed by that formula, even if defined only in terms of the protein sequence that the DNA molecules encode, while containing a large number of species, is definite in scope and provides the public notice required of patent applicants." *In re Wallach*, 71 USPQ2d 1939, 1942, no. 1 (CA FC 2004).

Indeed, MPEP § 2163 states:

> Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.

This appears precisely the basis of the decision made by the Federal Circuit in deciding *In re Deuel*, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995) ("The redundancy of the genetic code precluded contemplation of or focus on the **specific** cDNA molecules" [emphasis added]).

Consistently, in the instance, claims 4 and 5, drawn to a nucleic acid comprising a specific polynucleotide sequence encoding the amino acid sequence of the protein, are not rejected as being obvious over the prior art.

As noted above, Grey et al. et al. teaches, "[o]ur current efforts are directed toward cloning the gene for MSF and obtaining its complete sequence" (page 2441, column 1). There can be no reasonable doubt that at the time the application was filed, one ordinarily skilled in the art would have been motivated to isolate a nucleic acid molecule encoding the isolated protein. Indeed, "the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it". *In re Wallach*, 71 USPQ2d 1939, 1942, no. 1 (CA FC 2004). A rejection upon obviousness, where the prior art "contained detailed enabling methodology for practicing the claimed invention, and evidence suggesting that it would be successful" is appropriate. See *In re O'Farrell*, 853 F.2d 894, 903-904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

Furthermore, there is nothing intrinsically wrong in the application of methodology in the rejection of product claims under 35 U.S.C. § 103(a) depending on the particular facts of the case, the manner and context in which methodology applies and the overall logic of the rejection. See *Ex parte Goldgaber*, 41 USPQ2d 1173, 1176 (BPAI 1996) ("We find nothing intrinsically wrong, however, in the application of methodology in rejecting product claims under 35 USC 103, depending on the particular facts of the case, the manner and context in which methodology applies, and the overall logic of the rejection. Nor do we read *Bell* or *Deuel* as issuing a blanket prohibition against the application of methodology in rejecting product claims defining DNA or cDNA. Furthermore, precedent indicates that it is perfectly acceptable to consider the method by which a compound is made in evaluating the obviousness of the compound").

Given the state of the art, and the level of skill in the art, the knowledge of the ordinarily skilled artisan, etc., there would have been at least a reasonable expectation of success in isolating a nucleic acid molecule encoding a polypeptide comprising SEQ ID NO: 2. See MPEP § 2143.02. See *O'Farrell*.

Similar decisions have been made by the Board of Patent Appeals and Interferences. See, e.g., *Ex Parte Movva*, 31 USPQ2d 1027 (BPAI 1993).

However, then and now, it appears that the artisan of ordinary skill in the art would not have a reasonable expectation of success in isolating *specific* nucleic acid molecules comprising particular nucleotide sequences, such as the nucleic acid molecules of claims 4 or 5. Thus, while claims 1, 7-9, and 60 are appropriately rejected as being obvious over Grey et al., claims 4 and 5 are not.

Also of relevance, it is noted that it is perfectly acceptable to consider the method by which a compound is made in evaluating the obviousness of the compound. In determining obviousness, it is appropriate to consider such matters as the manner of preparation of the composition vis-a-vis the prior art, the structural similarities as well as differences between the claimed composition and that of the prior art and the presence or absence of properties which would unobvious in view of the prior art. See *In re Pilkington*, 411 F.2d 1345, 162 USPQ 145 (CCPA 1969); *In re Best*, 562, F.2d 1252, 195 USPQ 430 (CCPA 1977).

Furthermore, the Federal Circuit has recognized that a gene, being a chemical compound, could be defined "by its methods of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguished it (from other materials)." See *Amgen*, 927 F.2d 1200 at 1206, 18 USPQ2d at 1021 (Fed. Cir. 1991); *Fiers V. Sugano*, 984 F.2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993).

Finally, as noted in *In re Cofer*, 354 F.2d 664, 148 USPQ 268 (CCPA 1966), the particular structure or form of a chemical compound is an important consideration in determining obviousness under 35 USC 103; but it is not the only consideration. A compound may well be defined or described by characteristics other than its chemical structure. Although the artisan may be unaware of the exact chemical structure of a nucleic acid molecule encoding a protein of interest, he or she is aware that is it

composed of established relatively unchanging array of nucleotides. Importantly, he or she is also aware that all or part of the amino acid sequence of an isolated protein is readily determined, that a probe can be designed using the information acquired, which will hybridize with a nucleic acid molecule encoding the protein, and that established methodology, which was both routine and conventional at the time of the invention, is used to isolate the nucleic acid molecule encoding the protein by virtue of the selective hybridization of the probe to this nucleic acid molecule. Such technical procedures are taught in the prior art references of record, which have been employed by Applicant in the instant disclosure to enable the skilled artisan to make and use the claimed invention.

Applicant's arguments have thus been carefully considered but not found persuasive.

Conclusion

12. Claims 4, 5, and 29 are allowed; no other claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
December 4, 2006